

REMARKS

No claim amendments have been presented herein.

Accordingly, claims 2-9 in their previous form remain pending in the application.

Applicants acknowledge with gratitude the time taken by Examiners Le and Gabel to participate in a telephone interview with their agent to discuss the outstanding issues; the Examiners' input is much appreciated. The remarks herein are reflective of what was discussed during the interview and what the Examiners requested be put into a formal response to the outstanding Office Action.

The crux of the matter currently at issue lies in the relationship between the instant invention and the disclosure of the primary reference of Mengin-Lecreulx.

In the first place, Applicants note that the original prior art rejection was over the combination of Elhammer as primary reference in view of Mengin-Lecreulx and Kohlrausch as secondary references. This rejection was withdrawn in the wake of Applicants' arguments and replaced with two new prior art rejections, both invoking the same Mengin-Lecreulx reference, now as primary reference, in combination with the same Elhammer reference, now as secondary reference. The first outstanding rejection further invokes a new reference, Shinabarger, as secondary reference. The second outstanding rejection further

invokes the new Shinabarger reference, as well as the old Kohlrausch reference, as secondary references.

Applicants note further that the reasons given in the present Office Action for citing Mengin-Lecreux are virtually verbatim those set forth in the original rejection, which was since withdrawn. Similarly, the original reasons for citing Elhammer are also provided as reasons in the present Office Action; in the present Action, the Examiner further cites Elhammer for its teaching in connection with the scintillation proximity assay.

Thus, a reference previously cited as a secondary reference has now been made the primary reference, and it has been combined with what was formerly considered to be the primary reference, now considered to be a secondary reference. However, merely redesignating a secondary reference as a primary reference does not make it any more effective as a bar to patentability; again, no new reasons for citing the now-primary reference are provided.

In any event, as stated above and as discussed by Applicants' agent during the interview, what must be understood is the difference between the teaching of the Mengin-Lecreux reference and the assay claimed in the present application. The Examiner has made the assertion that Applicants' previous discussion of the secondary references is misguided in that the

arguments made do not relate to the reasons that the Examiner invoked said references in the first place. While there may be some merit in this assertion, the real point to understand in the end is that the assay claimed in the present application does not depend for its novelty and nonobviousness on the steps involving reaction termination and scintillation proximity assay. Thus the invocation of the secondary references as teaching these steps is immaterial to the analysis of patentability.

It should be reemphasized that the only thing "new" about the present rejections, compared to the prior, now-withdrawn rejection, is that Shinabarger has been invoked in addition to the references previously invoked. Shinabarger has been cited for its teaching of a scintillation proximity assay, more particularly one which employs beads coated with wheat germ agglutinin. It must also be reemphasized that Applicants are not asserting the patentability of their assay based solely on the use of SPA, under any conditions, in said assay. Thus, the three references that were found inadequate before have again been invoked, this time only with the additional teaching of Shinabarger, which teaching is not material to the novel and nonobvious aspects of the instantly claimed assay.

The goal of the present invention, and what certainly distinguishes it from the primary reference of Mengin-Lcreulx,

is summarized clearly on page 3, lines 21-25 of the specification. The patentability of the presently claimed invention lies principally in step 1 of the assay. Mengin-Lecreux is fundamentally deficient in teaching the aspects of this step, and, since the secondary references are cited because they disclose material relating to the subsequent steps, they are of no help in filling in the gaps in the teaching of the primary reference.

The first step of the instantly claimed assay is not at all an obvious variation of the teachings of Mengin-Lecreux, nor is it inherent in the teachings of this reference. Mengin-Lecreux discloses separate and independent assays for four of the enzyme activities involved in peptidoglycan synthesis, i.e., transfer of peptidoglycan precursors to membranes, translocase transfer activity, translocase exchange activity and transferase activity. (See page 4628, first column, Enzyme Assays (i)-(iv).) Each of these independent assays proceeds under different reaction conditions. Furthermore, each culminates in an involved, time-consuming solid-phase analytical step; assays (i), (ii) and (iv) require descending paper chromatography, while assay (iii) requires high-voltage paper electrophoresis.

Still further, Mengin-Lecreux was not interested in the full peptidoglycan synthetic pathway per se. The investigators' goal was to identify the product of the *E. coli murG* gene. Once

they had identified this product as the transferase, there was no interest in further study of the pathway. Consequently, Mengin-Lecreux is silent with respect to such subsequent steps as those catalyzed by transglycosylase and transpeptidase, enzymes which are clearly recited as part of the instantly claimed assay.

In contrast, the instantly claimed assay system not only incorporates these enzymes but involves total synthesis of the peptidoglycan end product. Furthermore, it affords detection of peptidoglycan synthesis without the undesirable solid-phase analytical steps of Mengin-Lecreux and allows the enzymatic reactions to be carried out in a single reaction mixture, with quantitation of products entirely in solution phase.

The Examiner has also asserted that components such as divalent metal ions, transglycosylase and transpeptidase, while not specifically taught by Mengin-Lecreux, inherently exist as building blocks necessary for synthesis of peptidoglycan and therefore are present in the teaching of Mengin-Lecreux. Whether or not this assertion is valid, it is true that Mengin-Lecreux makes no effort to exploit this alleged inherent coexistence of various components by providing a single assay system, or even a multiple assay system, that incorporates all the enzymatic reactions leading to complete synthesis of peptidoglycan. The same is true of the secondary references.

The Examiner asserts in the present Office Action that instant claim 2 cannot be said to exclude paper chromatography, since it recites the bridge term "comprising." However, it is inherent in the precise language of the instant claims that there is neither a paper chromatography step nor a high-voltage electrophoresis step, both of which are essential to Mengin-Lecreulx, whether or not these are specifically excluded by the instant claim language and whether or not the term "comprising" is open-ended. In fact, it would not be possible to link the discrete assays of Mengin-Lecreulx, with their solid-phase analytical steps, to steps 3) and 4) of the instant assay.

The inappropriateness of the Examiners' assessment notwithstanding, Applicants' agent had indicated informally to the Examiners prior to the interview that Applicants would be willing to work with them on claim language that could lay this issue to rest. During the interview, Applicants' agent asked, in the wake of the other issues discussed, if consideration need be given to such amendments to the claim language. However, the Examiners indicated that what was desired was a setting forth in this communication of the arguments provided during the interview by Applicants' agent and that no further amending of the claims need be implemented.

It is Applicants' understanding, then, that the above remarks are sufficient to lead to allowance of the application;

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such allowance is respectfully requested. Should any other matters require attention prior to allowance, it is respectfully requested that the Examiner contact the undersigned.

The Commissioner is hereby authorized to charge any fees which may be due in connection with this communication to Deposit Account No. 23-1703.

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Respectfully submitted,



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